

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

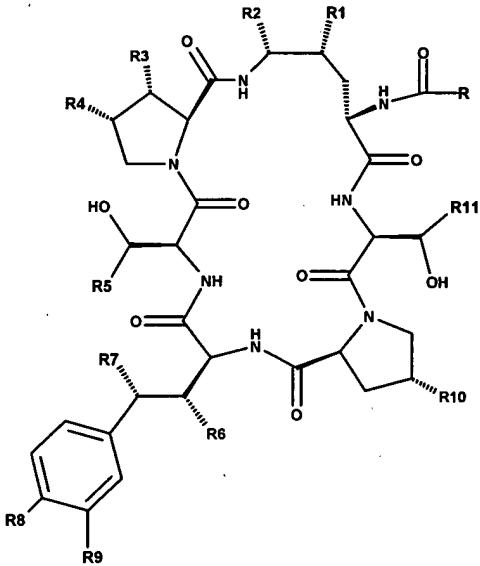
In the claims

Claim 1 (withdrawn): A parenteral pharmaceutical formulation comprising

- (i) an echinocandin compound, or a pharmaceutically acceptable salt thereof;
- (ii) a pharmaceutically acceptable micelle-forming surfactant; and
- (iii) a non-toxic, aqueous solvent

wherein said surfactant is present in said formulation at a weight ratio of echinocandin compound to micelle-forming surfactant from about 1:1.75 to about 1:25 and said echinocandin compound is present in an amount greater than or equal to 1 mg/ml.

Claim 2 (withdrawn): The formulation of Claim 1 wherein said echinocandin compound is represented by the following structure:



wherein:

R is an alkyl group, an alkenyl group, an alkynyl group, an aryl group, heteroaryl group, or combinations thereof;

R₁, R₂, R₃, R₆, R₇, and R₁₀ are independently hydroxy or hydrogen;

R₄ is hydrogen, methyl or -CH₂C(O)NH₂;

R₅ and R₁₁ are independently methyl or hydrogen;

R₈ is -OH, -OPO₃H₂, -OPO₃HCH₃, -OPO₂HCH₃, or -OSO₃H;

R₉ is -H, -OH, or -OSO₃H; and

pharmaceutically acceptable salts thereof.

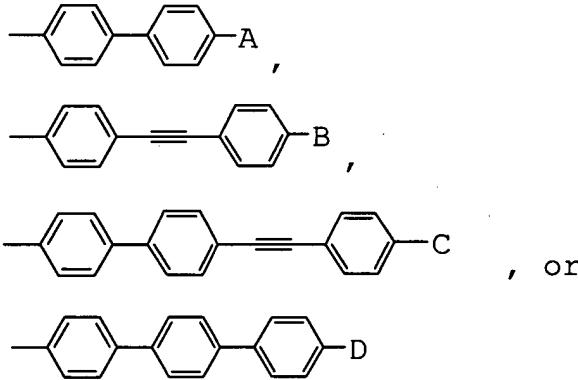
Claim 3 (withdrawn): The formulation of Claim 2 wherein

R₄, R₅ and R₁₁ are each methyl;

R₂ and R₇ are independently hydrogen or hydroxy; R₁, R₃, R₆ and R₁₀ are each hydroxy;

R₈ is -OH, -OPO₃HCH₃, or -OPO₂HCH₃;

R is linoleoyl, palmitoyl, stearoyl, myristoyl, 12-methylmyristoyl, 10,12-dimethylmyristoyl, or a group having the general structure:



where A, B, C and D are independently hydrogen, C₁-C₁₂ alkyl, C₂-C₁₂ alkynyl, C₁-C₁₂ alkoxy, C₁-C₁₂ alkylthio, halo, or -O-(CH₂)_m-[O-(CH₂)_n]_p-O-(C₁-C₁₂ alkyl) or -O-(CH₂)_q-X-E;

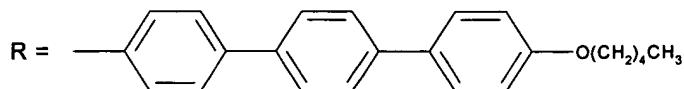
m is 2, 3 or 4;

n is 2, 3 or 4; p is 0 or 1; q is 2, 3 or 4;

X is pyrrolidino, piperidino or piperazino;

E is hydrogen, C₁-C₁₂ alkyl, C₃-C₁₂ cycloalkyl, benzyl or C₃-C₁₂ cycloalkylmethyl.

Claim 4 (withdrawn): The formulation of claim 3 wherein
 R₂ and R₇ are each hydroxy;
 R₈ is hydroxy; and

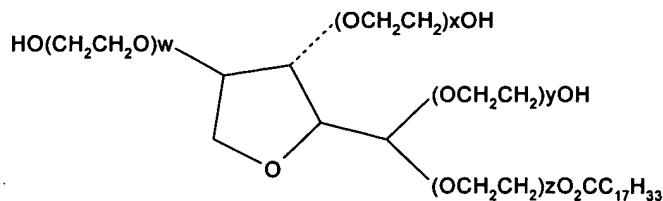


Claim 5 (withdrawn): The formulation of Claim 1 wherein said micelle-forming surfactant is selected from the group consisting of polysorbates, polyoxyethylene castor oil derivatives, polyoxyethylene stearates, sorbitan trioleate, bile salts, lecithin and combinations thereof.

Claim 6 (withdrawn): The formulation of Claim 1 wherein said echinocandin compound is present in an amount from about 1 mg/ml to about 50 mg/ml.

Claim 7 (withdrawn): The formulation of Claim 6 wherein said echinocandin compound is present in an amount from about 1 to about 30 mg/ml.

Claim 8 (withdrawn): The formulation of Claim 1 wherein said surfactant is represented by the following formula:



wherein x+y+z+w is equal to an integer between 5 and 20.

Claim 9 (withdrawn): The formulation of Claim 1 wherein said surfactant is present in an amount greater than 1% weight per volume.

Claim 10 (withdrawn): The formulation of Claim 1 wherein said weight ratio of echinocandin to surfactant is from about 1:2 to about 1:3.

Claim 11 (withdrawn): The formulation of Claim 1 wherein said solvent is selected from the group consisting of water, ethanol, propylene glycol, polyethylene glycols and mixtures thereof.

Claim 12 (withdrawn): The formulation of Claim 1 further comprising a stabilizing agent.

Claim 13 (withdrawn): The formulation of Claim 12 wherein said stabilizing agent is present in an amount from about 0.5% to about 10% by weight per volume.

Claim 14 (withdrawn): The formulation of Claim 12 wherein said stabilizing agent is present in an amount from about 1% to about 6% by weight per volume.

Claim 15 (withdrawn): The formulation of Claim 12 wherein said stabilizing agent is selected from the group consisting of mannitol, histidine, lysine, glycine, sucrose, fructose, trehalose, lactose and mixtures thereof.

Claim 16 (withdrawn): The formulation of Claim 1 further comprising a buffer.

Claim 17 (withdrawn): The formulation of Claim 16 wherein said buffer is selected from the group consisting of acetates, citrates, tartrates, lactates, succinates and phosphates and amino acids.

Claim 18 (withdrawn): The formulation of Claim 1 further comprising a tonicity agent.

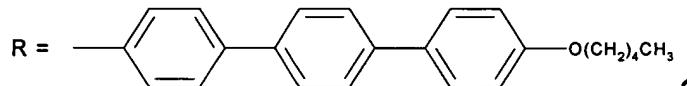
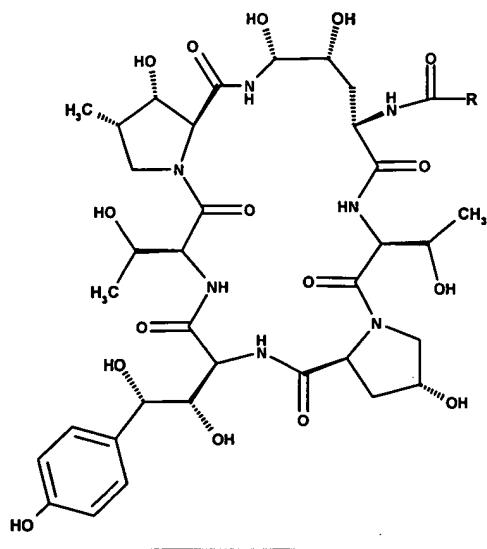
Claim 19 (withdrawn): The formulation of Claim 18 wherein said tonicity agent is selected from the group consisting of glycerin, lactose, mannitol, dextrose, sodium chloride, sodium sulfate and sorbitol.

Claim 20 (withdrawn): The formulation of Claim 18 wherein said tonicity agent is present in amount from about 1 to about 100 mg/ml.

Claim 21 (withdrawn): The formulation of Claim 18 wherein said tonicity agent is present in amount from about 9 to 50 mg/ml.

Claim 22 (currently amended): A freeze-dried formulation comprising
(i) an echinocandin compound, or a pharmaceutically acceptable salt thereof;
(ii) a pharmaceutically acceptable micelle-forming surfactant; and
(iii) a bulking agent[,]; and
(iv) a stabilizing agent,

wherein said micelle-forming surfactant is present in said freeze-dried formulation in an amount greater than 5% by weight and wherein said micelle-forming surfactant is a polysorbate, a polyoxyethylene castor oil derivative, a polyoxyethylene stearate or combinations thereof; and
wherein said echinocandin compound is represented by the following structure:



6 (a)

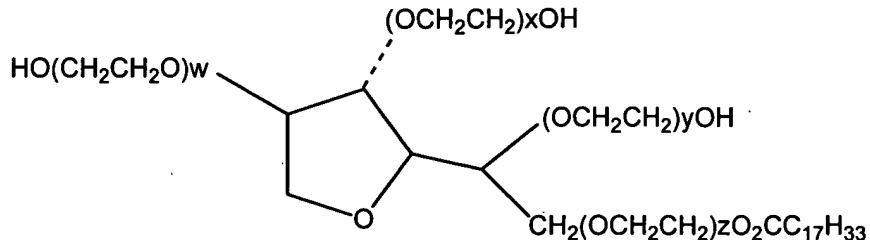
or a pharmaceutically acceptable salt thereof;

wherein said bulking agent is selected from the group consisting of mannitol, sucrose, trehalose, lactose, or and mixtures thereof[[,]] ; and and dextran, hydroxyethyl starch, ficoll and gelatin

wherein said stabilizing agent is sucrose, fructose, trehalose or mixtures thereof.

Claim 23-27 (cancelled)

Claim 28 (previously presented): The formulation of Claim 22 wherein said surfactant is represented by the following formula:



wherein x+y+z+w is equal to an integer between 5 and 20.

Claim 29 (currently amended): The formulation of Claim 22 wherein said surfactant is present in said formulation at a weight ratio of echinocandin to surfactant from ~~about~~ 1:1.75 to ~~about~~ 1:25.

Claim 30 (currently amended): The formulation of Claim 29 wherein said weight ratio of echinocandin to surfactant is from ~~about~~ 1:2 to ~~about~~ 1:3.

Claim 31 (withdrawn): A parenteral formulation comprising the freeze-dried formulation of Claim 22 and an aqueous solvent.

Claim 32 (cancelled):

Claim 33 (withdrawn – currently amended): The formulation of Claim 32 31 wherein said stabilizing agent is ~~selected from the group consisting of mannitol, histidine, lysine, glycine, fructose, sucrose, trehalose, lactose and or mixtures thereof.~~

Claim 34 (withdrawn – currently amended): The formulation of Claim 31 wherein said surfactant is present in said formulation at a weight ratio of echinocandin to surfactant from ~~about~~ 1:1.75 to ~~about~~ 1:25.

Claim 35 (withdrawn): The formulation of Claim 31 further comprising a buffer.

Claim 36 (withdrawn): The formulation of claim 35 wherein said buffer is selected from the group consisting of acetates, tartrates, citrates, phosphates and amino acids.

Claim 37 (withdrawn): A process for preparing a parenteral formulation comprising the step of mixing an echinocandin compound or an echinocandin/carbohydrate complex containing said echinocandin compound and a pharmaceutically acceptable micelle-forming surfactant in an aqueous solvent, wherein said micelle-forming surfactant is present in said formulation at a weight ratio of echinocandin compound to surfactant from about 1:1.75 to about 1:25 and said echinocandin compound is present in an amount greater than or equal to 1 mg/ml.

Claim 38 (withdrawn): The process of Claim 37 wherein said echinocandin compound is present in amount from about 1 mg/ml to about 50 mg/ml.

Claim 39 (withdrawn): The process of Claim 37 wherein said echinocandin compound is present in an amount from about 1 mg/ml to about 30 mg/ml.

Claim 40 (withdrawn – currently amended): A process for making a freeze-dried formulation comprising in the following order the steps of:

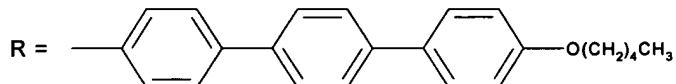
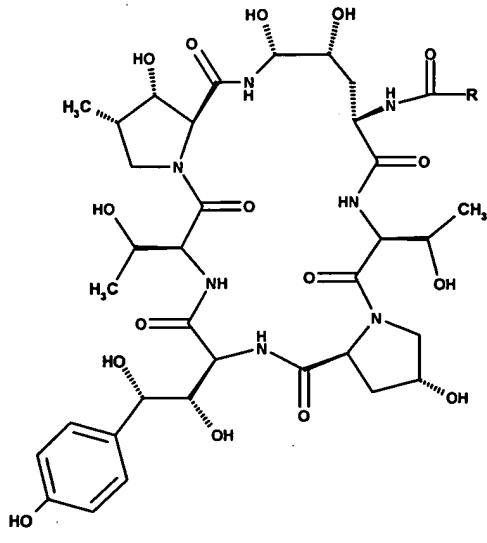
(i) dissolving into an aqueous solvent an echinocandin compound or echinocandin/carbohydrate complex containing said echinocandin compound in the presence of a pharmaceutically acceptable micelle-forming surfactant to form a solution, wherein said surfactant is present in an amount greater than 1% weight per volume of solution;

(ii) sterile filtering said solution; and

(iii) freeze-drying said solution;

wherein said micelle-forming surfactant is present in said freeze-dried formulation in an amount greater than 5% by weight and wherein said micelle-forming surfactant is a polysorbate, a polyoxyethylene castor oil derivative, a polyoxyethylene stearate or combinations thereof;

wherein said echinocandin compound is represented by the following structure:



6 (a)

or a pharmaceutically acceptable salt thereof;

further comprising the step of adding one or more bulking agents and one or more stabilizing agents before step (ii);

wherein said bulking agent is mannitol, sucrose, trehalose, lactose, or mixtures thereof; and

wherein said stabilizing agent is sucrose, fructose, trehalose or mixtures thereof.

Claim 41 (withdrawn – currently amended): The process of Claim 40 further comprising the step of adding one or more bulking agents, buffers, stabilizing agents, tonicity agents, or combinations thereof before step (ii).

Claim 42 (withdrawn – currently amended): The process of Claim 40 wherein said micelle-forming surfactant is selected from the group consisting of a polysorbate polysorbates,

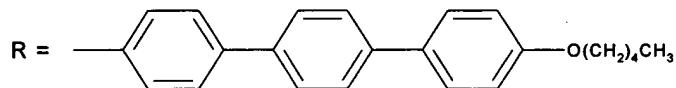
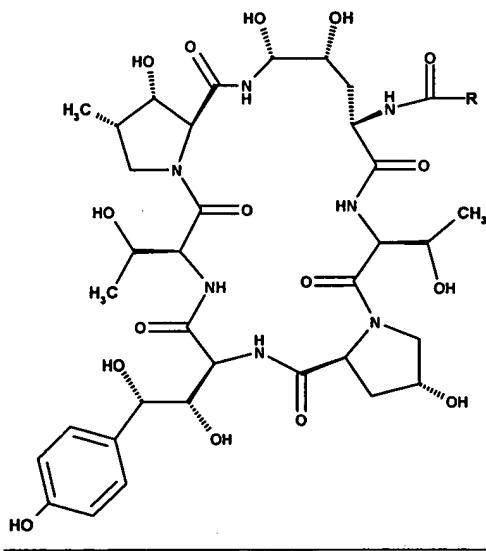
~~polyoxyethylene castor oil derivatives, polyoxyethylene stearates, sorbitan trioleate, bile salts, lecithin and combinations thereof.~~

Claim 43 (withdrawn – currently amended): A process for preparing a freeze-dried formulation comprising the steps of

- (i) buffering a non-toxic aqueous solvent to a pH between 4.0 and 5.5 to form a buffered solution;
- (ii) adding to said buffered solution a pharmaceutically acceptable, micelle-forming surfactant;
- (iii) cooling the solution from step (ii) to a temperature between 5° and 15°C to form a cooled solution;
- (iv) adding a slurry comprising an echinocandin compound or echinocandin/carbohydrate complex containing said echinocandin compound and a second non-toxic aqueous solvent to said cooled solution;
- (v) sterile filtering said solution from step (iv); and
- (vi) freeze-drying said solution from step (v);

wherein said micelle-forming surfactant is present in said freeze-dried formulation in an amount greater than 5% by weight and wherein said micelle-forming surfactant is a polysorbate, a polyoxyethylene castor oil derivative; a polyoxyethylene stearate or combinations thereof;

wherein said echinocandin compound is represented by the following structure:



6 (a)

or a pharmaceutically acceptable salt thereof;

further comprising the step of adding one or more bulking agents and one or more stabilizing agents before step (v);

wherein said bulking agent is mannitol, sucrose, trehalose, lactose, or mixtures thereof; and

wherein said stabilizing agent is sucrose, fructose, trehalose or mixtures thereof.

Claim 44 (withdrawn – currently amended): The process of Claim 43 wherein said temperature in step (iii) is from about 7°C to about 10°C.

Claim 45 (withdrawn – currently amended): The process of Claim 43 further comprising the step of adding one or more bulking agents, stabilizing agents, tonicity agents, or combinations thereof before step (v).

Claim 46 (withdrawn): A parenteral formulation comprising an aqueous solvent and a freeze-dried formulation prepared by the process of Claim 43.

Claim 47 (withdrawn): A parenteral pharmaceutical product prepared by (i) dissolving into an aqueous solvent an echinocandin compound or echinocandin/carbohydrate complex containing said echinocandin compound in the presence of a pharmaceutically acceptable micelle-forming surfactant to form a solution, wherein said surfactant is present in an amount greater than 1% weight per volume of solution; (ii) sterile filtering said solution; and (iii) freeze-drying said solution from step (ii) in a vial.

Claim 48 (withdrawn): The product of Claim 47 wherein the preparation of said product further comprising adding a non-toxic, aqueous solvent to said vial after step (iii).

Claim 49 (withdrawn): The product of Claim 47 wherein the weight ratio of echinocandin compound to surfactant is from about 1:1.75 to about 1:25.

Claim 50 (withdrawn): A method of treating an antifungal infection in a mammal in need thereof comprising the step of administering to said mammal a parenteral formulation of Claim 1.

Claim 51 (withdrawn – currently amended): A method of treating an antifungal a fungal infection in a mammal in need thereof comprising the step of administering to said mammal a parenteral formulation of Claim 31.

Claim 52 (withdrawn – currently amended): A method of treating an antifungal a fungal infection in a mammal in need thereof comprising the step of administering to said mammal a parenteral formulation of Claim 46.

Claim 53 (cancelled)

Claim 54 (withdrawn – currently amended): The formulation of Claim 53 22 wherein said stabilizing agent is present in an amount from ~~about~~ 0.5% to ~~about~~ 10% by weight per volume.

Claim 55 (withdrawn – currently amended): The formulation of Claim 53 22 wherein said stabilizing agent is present in an amount from ~~about~~ 1% to ~~about~~ 6% by weight per volume.

Claim 56 (cancelled)

Claim 57 (withdrawn): The formulation of Claim 22 further comprising a buffer.

Claim 58 (withdrawn): The formulation of Claim 57 wherein said buffer is selected from the group consisting of acetates, citrates, tartrates, lactates, succinates and phosphates and amino acids.

Claim 59-60 (cancelled)

Claim 61 (currently amended): The formulation of ~~Claims 60~~ Claim 22, wherein said bulking agent is mannitol.

Claim 62 (withdrawn – currently amended): The formulation of ~~claim 56~~ Claim 22, further comprising a buffer and,

wherein said stabilizing agent is fructose, said bulking agent is mannitol, and said micelle forming surfactant is a polysorbate.

Claim 63 (new): The formulation of Claim 62 where said buffer is a citrate, acetate or tartrate.

Claim 64 (new): The formulation of Claim 28 wherein said micelle-forming surfactant is polysorbate 80, polysorbate 20 or polysorbate 40.

Claim 65 (new): The formulation of Claim 22 wherein said stabilizing agent is fructose.

Claim 66 (new): The formulation of Claim 61 wherein said stabilizing agent is fructose.

Claim 67 (new): The formulation of Claim 64 wherein said stabilizing agent is fructose.

Claim 68 (new): The formulation of Claim 22 wherein said bulking agent is mannitol, and said micelle-forming surfactant is a polysorbate.

Claim 69 (new): The formulation of Claim 22 wherein said stabilizing agent is fructose, said bulking agent is mannitol, and said micelle forming surfactant is a polysorbate.

Claim 70 (new): The formulation of Claim 22 wherein said echinocandin compound is present prior to freeze drying at a concentration from 1 mg/ml to 30 mg/ml.

Claim 71 (new): The formulation of Claim 22 wherein said echinocandin compound is present prior to freeze drying at a concentration from 8 mg/ml to 12 mg/ml.

Claim 72 (new): The formulation of Claim 69 wherein said echinocandin compound is present prior to freeze drying at a concentration from 1 mg/ml to 30 mg/ml.

Claim 73 (new): The formulation of Claim 69 wherein said echinocandin compound is present prior to freeze drying at a concentration from 8 mg/ml to 12 mg/ml.